

REMARKS

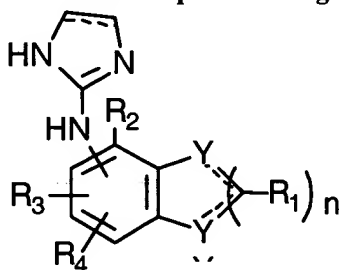
Applicants are in receipt of the Examiner's Action dated November 22, 2004, and have the following comments. Independent claims 1 and 14 have been amended to more accurately point out that the combination of the invention is neuroprotective.

Rejection of Claims 21-27 under 35 USC 112(1)

The Examiner has again alleged that claims 21-27 lack enablement as required by 35 USC 112, first paragraph. Applicants respectfully traverse this rejection.

Claim 21 is drawn to:

21) A method of preventing degeneration of the optic nerve and providing protection of the retinal ganglion cells of a mammal, comprising administering to the mammal a therapeutically effective amount of a prostaglandin and a therapeutically effective amount of an alpha adrenergic agent of formula (I)



formula (I)

wherein each Y is independently selected from the group consisting of N, N-CH₃, O, S and C-R₁; R₁ is hydrogen, lower alkyl or oxo; R₂, R₃ and R₄ are independently selected from the group consisting of hydrogen, halogen, lower alkyl and lower alkenyl; n is an integer from 1 to 3; and a broken line beside a solid line indicates either a single or a double bond, provided that two double bonds are not on the same carbon in the case when n=1, and their pharmaceutically acceptable salts and esters as appropriate.

It is undisputed that the person of ordinary skill in the art would recognize that the claims are drawn to the use of the drug brimonidine (or derivatives thereof) and prostaglandins, and know how to combine the two ingredients in a single formulation, or administer it. To that end, the Examiner has not claimed that such a person would not know how to assemble the ingredients for use in the claimed methods, or to administer them to a patient in need thereof.

Instead, in a single sentence rejection, the Examiner simply repeats the rejection and refers to the Office Action of February 20, 2003. However, the referenced Office Action simply cites In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988), and states that 'Applicant fails to set forth the criteria that define 'prevention of optic nerve' and 'protection of the retinal ganglion cells'. See Office Action, page 3. The Examiner appears to feel the rejection is particularly warranted due to the lack of working examples.

Applicants respectfully disagree and incorporate their response of the Reply of June 26, 2003 herein by reference. Additionally, Applicants would point out that methods such as histopathological analysis of the retina (for example, retinal thickness), and the integrity of the optic nerve in the eyes of experimental animals (e.g., those given a specific drug or combination and those given a placebo), have been conducted for years. It would be a simple matter to compare the prophylactic activities of the combination of prostaglandins and brimonidine derivatives on retinal and optic nerve health in glaucomatous animals, or in animals upon whom a neurologically traumatic medical procedure such as LASIK has been performed. The results of such studies could easily be extrapolated to man. That the methods of the present invention may be performed on such a population of patients is clearly taught in the present application: see e.g., page 7 and 8.

For these reasons Applicants respectfully maintain that the Examiner has not met the burden of establishing a prima facie case that the claims lack enablement by the specification, particularly in light of the state of the art known to the person of ordinary skill at the time of the invention.

Rejection pursuant to 35 USC Section 101

The Examiner has rejected claim 7 under 35 USC 101, as allegedly claiming the same invention as that of claim 1 of US Patent 6,294,563. The Examiner is correct, and Applicants have accordingly cancelled claim 7. As a result, Applicants believe this ground of rejection is now moot.

Rejection pursuant to 35 USC 103(a)

Claims 1-6 and 14-27 are now rejected as allegedly unpatentable over Gluchowski (US Patent 5,091,528) and Bishop (US Patent 5,510,398). Applicants respectfully traverse this rejection.

Independent claims 1 and 14 have now been amended to clarify that the prostaglandin and alpha 2 adrenoreceptor agonist are present in a combination containing therapeutically effective amounts of each sufficient to provide neuroprotection to ocular neural tissue.

The Examiner states that Gluchowski teaches the use of brimonidine for the treatment of glaucoma, and that Bishop teaches the use of the claim-designated prostaglandins for the treatment of glaucoma. Therefore, the Examiner concludes, it would have been *prima facie* obvious for one of ordinary skill in the art to incorporate a prostaglandin into the composition of the primary reference, presumably in concentrations effective for the treatment of glaucoma.

However, a composition comprising a combination of a prostaglandin and an alpha 2 adrenoreceptor agonist is not disclosed or suggested in either of the cited references, nor is there any suggestion in either reference (or the combination of these references) of either of these components being present in therapeutically effective amounts sufficient to provide neuroprotection to ocular neural tissue. As the claims must be considered as a whole when compared to the prior art, 35 USC 103(a), Applicants submit that when the claims are so compared it can be clearly seen that none of the present claims are *prima facie* obvious over the combination of Gluchowski and Bishop.

The Examiner states that the fact that the present application is drawn to the heretofore unappreciated neuroprotective advantages of a combination of a prostaglandin and an alpha 2 adrenergic such as brimonidine does not have a bearing on the patentability of the invention. However where, as here, the claims are expressly drawn to i) a combination having the ingredients present in therapeutically effective amounts sufficient to provide neuroprotection to ocular tissue (claim 1), b) an article of manufacture comprising such a combination and packaging material comprising a label which indicates that said combination can be used for neuroprotection (claim 14), and a method of preventing degeneration of the optic nerve and providing protection of the retinal ganglion cells of a mammal (claim 21).

The Examiner has cited various cases which recite the well-known rule that previously

unknown but inherent properties of a known composition cannot be considered novel or non-obvious. E.g., *Bristol-Myers Squibb Co. v. Ben-Venue Laboratories, Inc.*, 58 USPQ2d 1508 (Fed. Cir. 2001), *In re Baxter Travenol Labs*, 21 USPQ2d 1281 (Fed. Cir 1991). However, here the composition claims are not just disclosing an intended use, but contain concrete limitations (e.g., amount, packing materials), which are specific to the neuroprotective properties of the combination.

Regarding method claim 21, it is black letter law that there can be no inherency unless the currently claimed use inevitably results from the practice of the prior art method. In this case in emphatically does not. The cited prior art does not use (or suggest the use of) a combination comprising an alpha adrenergic and a prostaglandin, so there is no prior use of this combination in the art.

Thus, Applicants respectfully maintain that the claims are not obvious over the cited references.

CONCLUSION

For the above reasons, Applicants believe that the present claims are in condition for allowance. Kindly use our Deposit Account No. 01-0885 for payment of any fees, including extension fees, required in connection with this reply.

Respectfully submitted,

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